

Gene Section

Mini Review

PLAGL2 (pleomorphic adenoma gene-like 2)

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Identity

Hugo: PLAGL2

Other names: FLJ23283; KIAA0198

Location: 20q11.21

DNA/RNA

Description

PLAGL2 (PLAG-Like 2; a PLAG family member; GenBank accession number AF006005) was identified by homology searches of the database of expressed sequence tags (ESTs) and sequence similarity to zinc-finger region of the human PLAGL1/LOT1/ZAC1 and PLAG1 proteins.

Protein

Description

PLAGL2 protein consists of 496 amino acid residues, six C2H2-type zinc finger domains in its amino-terminal region (shown as brown in the figure), and a proline- and serine-rich carboxyl terminus (shown as blue).

Expression

Northern analysis showed that the PLAGL2 mRNA is expressed in fetal kidney, liver, lung, and brain but not in adult tissues. However, PCR analysis showed that PLAGL2 is ubiquitously expressed in almost all adult and fetal human tissues, except for the relatively low level of expression observed in fetal brain.

Localisation

Nuclear.

Function

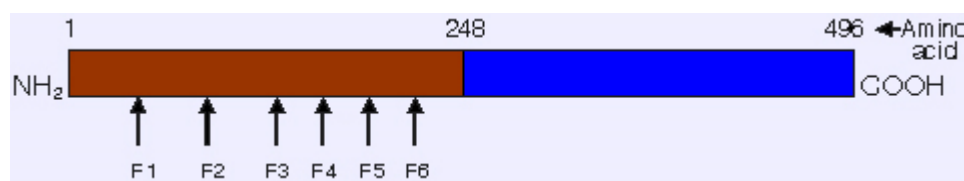
PLAGL2 can bind and activate human insulin-like growth factor II (IGF II) gene promoter; therefore, the oncogenic capacity of PLAGL2 may be mediated by activating the IGF-II mitogenic pathway. However, PLAGL2, possibly by association with HIF-1, may also have apoptotic role since it can activate Nip3 promoter and induce transcription in Balb/c3T3 fibroblasts and Neuro2a neuroblastoma cells, leading to apoptosis. PLAGL2 mRNA can be induced upon iron deficiency or hypoxia in mouse macrophage cell line RAW264.7, mouse erythroleukemia (MEL) cells, and Balb/c3T3 cells.

PLAGL2 Exons:



Exon	GenBank NM_002657	GenBank NT_028392
1	1 - 103	991578 - 991529
2	104 - 477	986189 - 985812
3	478 - 5656	981581 - 976399

PLAGL2 exons and corresponding nucleotide numbers on each GenBank sequence database are shown in this table.



In addition, PLAGL2 can also transactivate the surfactant protein-C (SP-C), a protein whose expression occurs principally in type II pneumocytes located in the distal lung alveolae. Additional data suggest that repression of the transactivating capacity of PLAGL2 may be directly related to sumoylation. Also, PLAGL2 protein is acetylated and activated by p300 and deacetylated and repressed by HDAC7, involving the lysine residues as the acetylation target. Therefore, it appears that the activity of PLAGL2 is tightly modulated by both sumoylation and acetylation, which may have opposite effects on their transactivation. Tip60 can modulate PLAGL2 function through both acetylation and inhibition of sumoylation, resulting in an enhanced PLAGL2-mediated transactivation. PLAGL2 can bind and stabilize (by preventing proteasomal degradation) Pirh2 dimer, a p53 inducible E3 ligase involved in the ubiquitination of p53. PLAGL2 can also regulate NCF2 gene expression through binding to the tumor necrosis factor (TNF)-alpha-responsive region of the NCF2 promoter, thus regulating p67(phox) expression and NADPH oxidase activity. PLAGL2 was recently found to aid in the efficient uptake of chylomicrons by intestinal lacteal vessels.

Homology

Homologous to the human PLAG1 and PLAGL1 proteins.

Mutations

Note: Mutation has not been reported in the PLAGL2 coding region.

Implicated in

Carcinogenicity

Note: PLAGL2 is an oncoprotein involved in various malignancies including lipoblastomas, hepatoblastomas, and acute myeloid leukemia. PLAGL2 expression is increased in human cancers including acute myeloid leukemia (AML). The expression is increased in 20% of human AML samples. The PLAGL2 gene can independently cooperate with Cbfb-MYH11 fusion gene in leukemogenesis. AML subtype M4 with eosinophilia is associated with a chromosome 16 inversion that creates a fusion gene Cbfb-MYH11, encoding Cbfbeta-SMMHC fusion protein. This fusion protein inhibits the

core-binding factor (CBF), resulting in a block of hematopoietic differentiation and induction of leukemia in the presence of additional mutations.

Disease

Cancer; lipoblastomas, hepatoblastomas, and acute myeloid leukemia.

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